

- FIG. 1.—Transverse section through the abdominal chromaphil body of the dog. Fixed in corrosive sublimate and stained with hæmatoxylin. Section 10μ in thickness. Leitz, obj. 6. Drawing ocular.
- FIG. 2.—Section through the medulla of the adrenal of a dog, prepared as in case of previous figure. Same magnification.
- FIG. 3.—Section through a group of chromaphil cells in the inferior cervical ganglion of the dog. Fixed in Kohn's fluid (bichromate-formol, see text). Leitz, $\frac{1}{2}$ " oil immersion. Drawing ocular.
- FIG. 4.—Transverse section through the abdominal chromaphil body of the dog. Fixed in Kohn's fluid (*v. supra*), stained with hæmatoxylin. Leitz, $\frac{1}{2}$ " oil immersion. Drawing ocular.
- FIG. 5.—Section through the medulla of the adrenal of a dog. Kohn's fluid. Hæmatoxylin. Leitz, obj. 6. Drawing ocular.
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On the Occurrence of a Mesocælic Recess in the Human Brain, and its Relation to the Sub-Commissural Organ of Lower Vertebrates; with special reference to the Distribution of Reissner's Fibre in the Vertebrate Series and its possible Function.

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[PLATE 14.]

I. Introductory.

Eight years ago one of us (Dendy, 1902) published in the 'Proceedings' of the Royal Society a description of a peculiar structure lying beneath the posterior commissure in the brain of the Ammocete, in the shape of a pair of longitudinal grooves lined by greatly elongated and apparently ciliated columnar cells, and evidently formed by specialisation of the ependymal epithelium which lines the cavity of the brain. Previous to this time there appear to have been, at the most, only a few scattered references to the occurrence of any such structure in the vertebrate brain. We now know, however, that it occurs throughout the whole vertebrate series, from the lampreys to the primates, it having recently been figured, in the case of *Macacus*, by Sir Victor Horsley (1908).

Sargent (1903) has given to this structure the name "Ependymal Groove," and has described it in a number of Ichthyopsidan types. He says, however (1903, 1904), that it is inconspicuous in mammals. We ourselves have recently observed it in a number of different forms. It is very well developed, for example, in *Sphenodon*, and we find it also strongly developed in the mouse and the cat. Sargent showed, further, that the "ependymal groove" is intimately connected with the anterior end of Reissner's fibre, and in fact regarded it merely as a kind of attachment plate for the latter. We also have been able to demonstrate quite clearly its connection with Reissner's fibre in a large number of types, *e.g.* *Geotria* (Dendy, 1907) and *Rana* (Nicholls, 1908). We shall discuss its possible function later on in the present communication; but, in the meantime, we may state that we do not consider that the term "ependymal groove" is sufficiently distinctive for so remarkable and constant a feature of the vertebrate brain, for it is, of course, not the only ependymal groove present. Inasmuch as it lies beneath the posterior commissure, we propose to speak of it in future as the "Sub-Commissural Organ." It appears primarily to be made up of two bands of columnar epithelium, usually more or less completely united together in the form of a groove; but, whereas it remains throughout life in a well developed condition in all the lower vertebrates, in man, as we shall endeavour to show in the present communication, it becomes reduced in the adult to a mere vestige sunk in the brain tissue at the back of the posterior commissure, but unmistakably recognisable as the homologue of the sub-commissural organ of lower types.

II. *The Sub-Commissural Organ in the Mouse, Cat, and Chimpanzee.*

As the sub-commissural organ is as yet very little known, we propose, for purposes of comparison, to give a short description of it as it occurs in the mouse, the cat, and the chimpanzee, which form a series leading up to the vestigial condition in the human brain. We believe the organ in question has never yet been described in any of these types, nor, indeed, has a complete description of it been given for any mammal.

Mouse.—In a sagittal section of the brain of the common house-mouse, such as is represented in text-fig. 1, we see the infra-pineal recess (*i.p.r.*) projecting upwards and backwards between the posterior (*p.c.*) and superior (*s.c.*) commissures, and leading to the elongated pineal gland (*p.g.*). In front of the superior commissure the roof of the third ventricle is produced upwards and backwards to form the supra-pineal recess (*s.p.r.*), a narrow diverticulum which lies parallel to the infra-pineal recess and pineal gland, and which is doubtless homologous with the dorsal sac of lower types. The

wall of the supra-pineal recess is greatly folded to form a choroid plexus (*c.p.*), and above and below it lie large veins (*v*). The lower surface of the posterior commissure is covered, in the middle line, by the peculiar high columnar

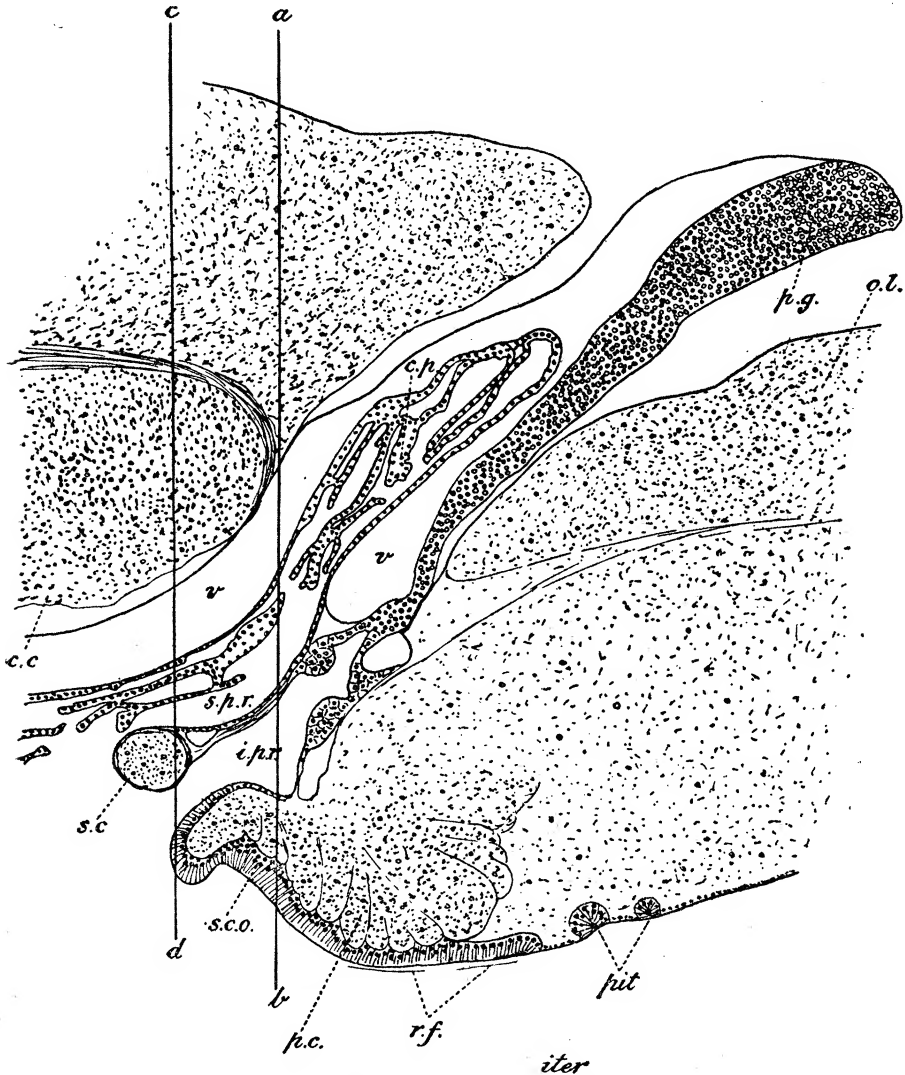


FIG. 1.—Mouse. Sagittal Section through the Region of the Posterior Commissure, &c. $\times 60$. (The lines *ab*, *cd*, indicate approximately the planes of the transverse sections represented in figs. 2 and 3.)

c. c., corpus callosum ; *c. p.*, choroid plexus ; *i. p. r.*, infra-pineal recess ; *o. l.*, optic lobe ; *p. c.*, posterior commissure ; *p. g.*, pineal gland ; *pit*, isolated invaginated patches of the epithelium of the sub-commissural organ ; *r. f.*, Reissner's fibre ; *s. c.*, superior commissure ; *s. c. o.*, sub-commissural organ ; *s. p. r.*, supra-pineal recess ; *v.*, veins.

epithelium of the sub-commissural organ (*s.c.o.*), which is continued round the anterior end of the posterior commissure for a short distance on to the floor of the infra-pineal recess, where it gradually loses its columnar character. Beneath the epithelium are seen portions of Reissner's fibre (*r.f.*), whose branches, no doubt, are connected with the epithelial cells as in lower types, and as in the cat to be described later on.

It will be noticed that the epithelium of the sub-commissural organ is thrown into a transverse fold near its anterior end, just before it turns round over the anterior end of the posterior commissure. Towards its hinder extremity it appears to become discontinuous, and two little separate islands

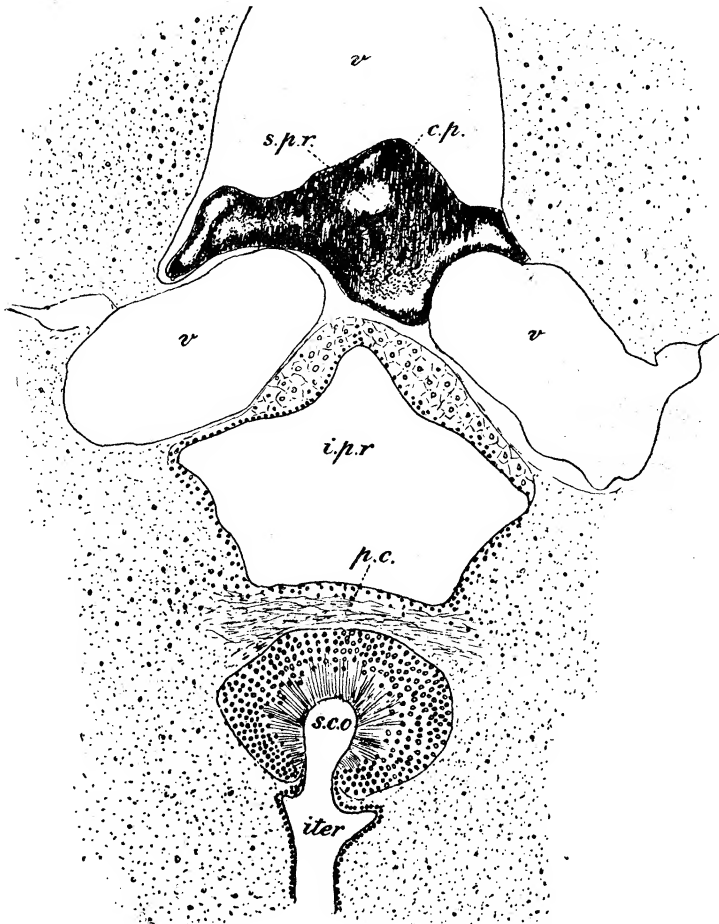


FIG. 2.—Mouse. Transverse Section through the Region of the Posterior Commissure, taken at about the level of the line *ab* in fig. 1. $\times 105$.

c.p., choroid plexus ; *i.p.r.*, infra-pineal recess ; *p.c.*, posterior commissure ; *s.c.o.*, sub-commissural organ ; *s.p.r.*, supra-pineal recess ; *v.*, veins.

are formed, which have become partially invaginated into the underlying tissues of the brain in the form of small pits (*pit*).

The transverse sections represented in text-figs. 2 and 3 will serve to further elucidate the relations above described. The lines *ab* and *cd* in text-fig. 1 indicate approximately the levels at which these two sections are

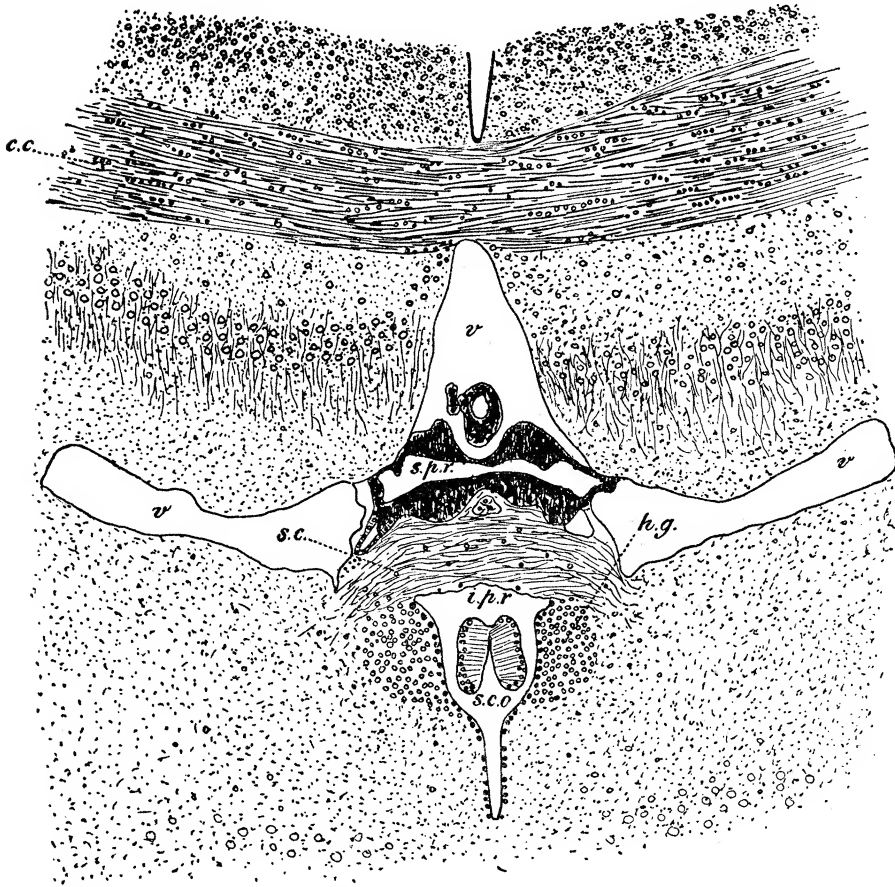


FIG. 3.—Mouse. Transverse Section through the region of the Superior (Habenular) Commissure at about the level of the line *cd* in fig. 1. $\times 60$.

c. c., corpus callosum; *h. g.*, habenular ganglion; *i. p. r.*, infra-pineal recess; *s. c.*, superior commissure; *s. c. o.*, sub-commissural organ; *s. p. r.*, supra-pineal recess; *v.*, veins.

taken (all the sections are, of course, drawn from actual preparations). In these sections we may confine our attention to the sub-commissural organ (*s.c.o.*). Text-fig. 2 shows this organ in the form of a very conspicuous horseshoe-shaped groove, lined by greatly elongated columnar cells and very sharply marked off from the ordinary ependyma of the *iter* below it, the latter

exhibiting a characteristic fold on either side where it joins the former. The cells of the sub-commissural organ are probably provided with cilia, but this is not evident in our preparations. The epithelium shows a strong tendency to split longitudinally at the bend of the horseshoe, which possibly indicates its paired character. A further indication of this paired character is seen in the section represented in text-fig. 3, where the epithelium is cut through quite separately and in two almost detached patches, as it projects from the anterior surface of the posterior commissure.

It is thus evident that in the mouse the sub-commissural organ is a very conspicuous structure, which probably has some important function connected with the associated Reissner's fibre.

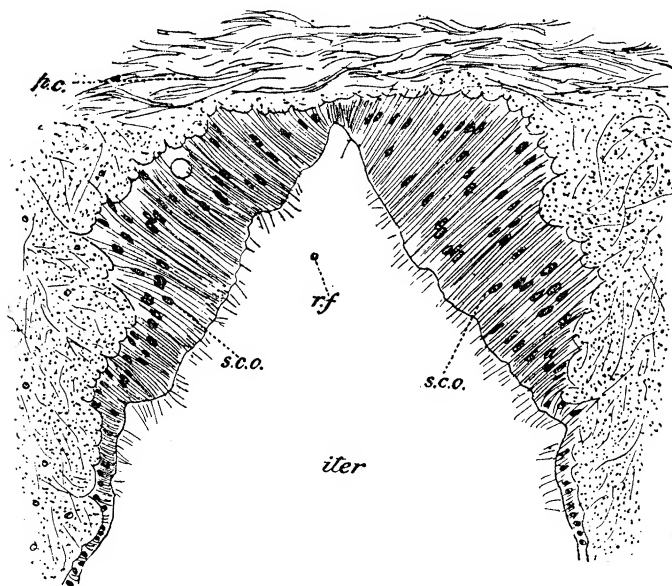


FIG. 4.—Cat. Transverse Section through the Sub-Commissural Organ in the Region of the Posterior Commissure. $\times 320$.

p. c., posterior commissure ; *r. f.*, Reissner's fibre ; *s. c. o.*, sub-commissural organ.

The Cat.—In the cat the sub-commissural organ is not so well defined as it is in the mouse, but still very obvious, as will be seen from the transverse section represented in text-fig. 4. Here the double character of the organ is very well seen ; it is clearly made up of two bands of greatly elongated ependymal cells, right and left, and these cells appear to be distinctly ciliated. Reissner's fibre (*r.f.*), which can be traced for a long distance through this series of sections, is clearly seen lying in the groove between the two halves of the sub-commissural organ. Text-fig. 5 represents another section from the same series, but near the anterior end of the sub-commissural

organ. The epithelium is seen to be losing its characteristic columnar appearance, especially in the middle line, but Reissner's fibre is still present, and, indeed, in this and neighbouring sections may be seen breaking up into branches, which actually run to the epithelium.

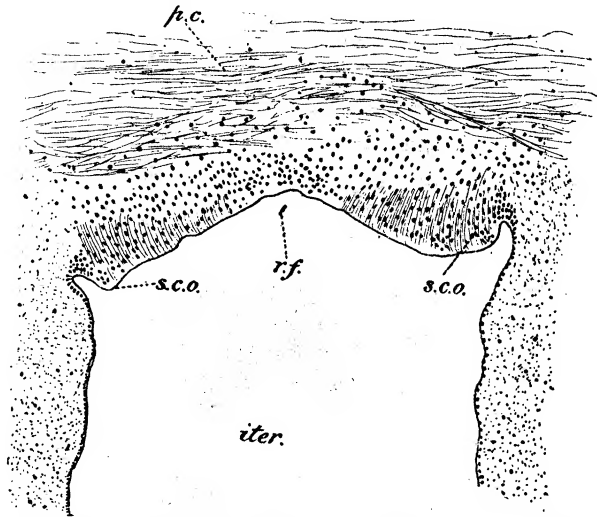


FIG. 5.—Cat. Transverse Section through the Region of the Posterior Commissure considerably anterior to the section shown in fig. 4. $\times 125$.

p. c., posterior commissure; *r. f.*, Reissner's fibre; *s. c. o.*, sub-commissural organ.

The Chimpanzee.—Here, again, we have studied the sub-commissural organ by means of serial transverse sections. The entire brain had been hardened *in situ* by means of formalin and alcohol for ordinary anatomical purposes. It is naturally not in a good condition for the study of minute histological details, but shows very clearly the general form and relations of the parts under discussion.

The sub-commissural organ commences, as in the mouse, on the antero-dorsal aspect of the posterior commissure, where the latter forms the floor of the infra-pineal recess (compare text-fig. 1), where, however, it is very feebly developed. It can be followed backwards beneath the posterior commissure as a broad and very shallow groove (Plate 14, fig. 1, *s.c.o.*), the epithelium of which shows the nuclei arranged in several layers, but does not exhibit the typical differentiation until we come to about the hinder limit of the posterior commissure (text-fig. 6). Here the sub-commissural organ takes the form of two separate bands of the characteristic high columnar epithelium, which become invaginated into the roof of the *iter*, just behind the posterior commissure. This invagination (*m.r.*) turns forwards above the posterior commissure, where it is seen in the transverse section represented in Plate 14, fig. 1, the two epithelial bands having met

together and completely surrounded the recess thus formed. This recess ends blindly in front at a distance of about 0.225 mm. from the point where it turns forwards above its opening into the *iter*. It has an internal diameter of about 0.25 mm. The enormously elongated, almost fibre-like cells by which it is surrounded measure about 0.057 mm. in length, and their nuclei are situated towards their inner ends. Though not in a good state histologically, it is evident that they agree closely in character with the corresponding cells in the cat and mouse.

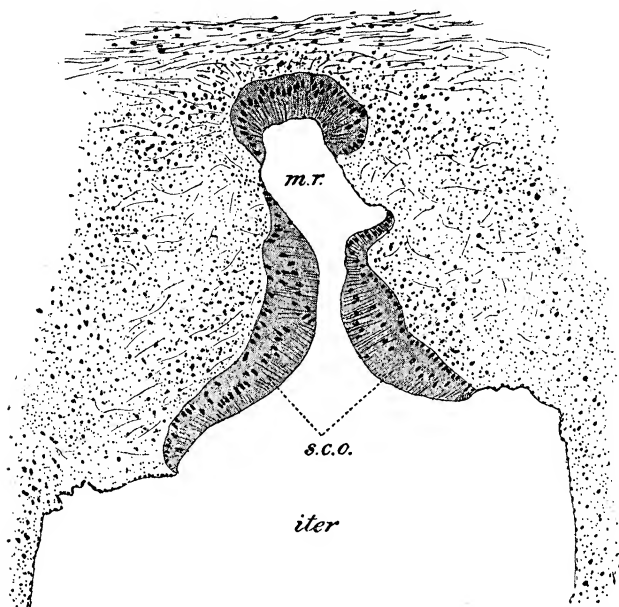


FIG. 6.—Chimpanzee. Transverse Section through the Sub-Commissural Organ at the Posterior End of the Posterior Commissure. $\times 60$.

m. r., mesocœlic recess; *s. c. o.*, sub-commissural organ.

This recess, which forms a very conspicuous feature in transverse sections of the chimpanzee's brain, corresponds in position with what Sargent (1904) has termed the *recessus mesocœlicus* in the sea lamprey (*Petromyzon marinus*), where also he regards it as part of the sub-commissural organ (Ependymal Groove). Stieda long ago (1870, fig. 15) figured a similar recess above the posterior commissure in the frog's brain, but without recognising its significance. Gaupp (1899, fig. 17) also figures this recess in the frog, and terms it the "diverticulum impar."

We have already noticed in the mouse a tendency on the part of the epithelium of the sub-commissural organ to become invaginated behind the posterior commissure, so that this tendency would appear to be very general

throughout the vertebrate series. It is possible that in all cases the invagination may be apparent rather than real, and due to overgrowth of the sub-commissural organ by the surrounding tissues.

We have found no trace of Reissner's fibre in the chimpanzee, but it was hardly to be expected in material preserved merely for anatomical purposes.

III. *The Sub-Commissural Organ in Man.*

A mesocœlic recess, evidently homologous with that of the chimpanzee, but very much smaller, is readily recognisable in transverse sections of the adult human brain, where it appears to constitute the last vestige of the sub-commissural organ, while in the five months' foetus this organ is still fairly well developed.

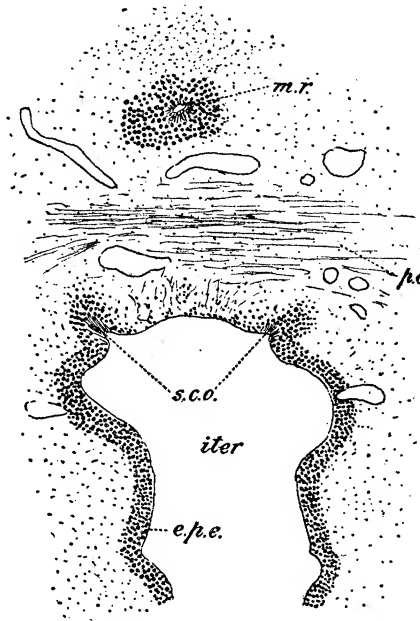


FIG. 7.—Human foetus of about five months. Transverse section through the Region of the Posterior Commissure. $\times 60$.

e.p. e., ependymal epithelium of *iter* ; *m. r.*, mesocœlic recess ; *p. c.*, posterior commissure ; *s.c. o.*, sub-commissural organ.

In the foetus the sub-commissural organ is, indeed, rather better developed than in the chimpanzee. As in that animal, it begins anteriorly in the infra-pineal recess, where the characteristic high columnar epithelium, with deeply-seated nuclei, is well marked. As it is traced backwards around the curve of the posterior commissure its paired nature becomes evident. The two halves diverge, and come to lie widely separated in the roof of the

iter, forming a pair of small shallow grooves, as shown in text-fig. 7. Laterally these grooves are not clearly marked off from the general endyma, which, as is well known, is much more strongly developed in the foetus than in the adult, but is distinguished from the epithelium of the grooves by the much more superficially-placed nuclei. Mesially the edges of the grooves become more sharply defined (text-fig. 7), the endyma having practically disappeared from beneath the commissure between the grooves (compare cat, text-fig. 5).

Towards the hinder end of the posterior commissure these two grooves unite again and become invaginated into the roof of the *iter* to form a mesocœlic recess exactly comparable to that already described in the chimpanzee, but more widely open below (text-fig. 8).

This recess is lined throughout by the characteristic endyma of the sub-commissural organ, and tunnels forwards into the brain tissue above the posterior commissure for a distance of about 0.35 mm. Its full length is rather greater than this owing to the tube becoming bent back upon itself for about 0.06 mm. to its blind termination.

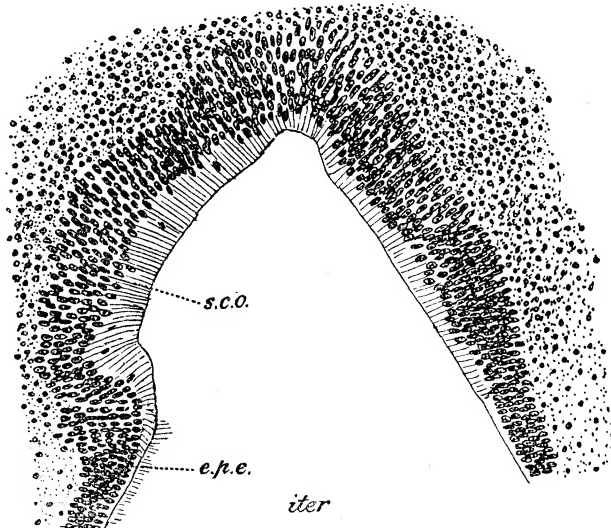


FIG. 8.—Human foetus of about five months. Transverse Section through the Sub-commissural Organ at the Posterior End of the Posterior Commissure. $\times 154$.
e.p.e., ependymal epithelium of the *iter*; s.c.o., sub-commissural organ.

The diameter of the recess, as seen in text-fig. 9, is only about 0.02 mm., the recess being in this case much longer than wide—in fact, distinctly tubular. The lumen of the tube is somewhat triangular in transverse section (text-fig. 9), widening suddenly to its opening behind (text-fig. 8).

The elongated, radially arranged cells lining the recess are about 0.02 mm. in length.

Behind the recess the ependyma of the sub-commissural organ passes gradually into the general ependyma of the *iter*.

In sections through the region of the posterior commissure in the brain of the adult human subject the sub-commissural organ is seen to have almost entirely vanished. The ependyma covering the ventral surface of the

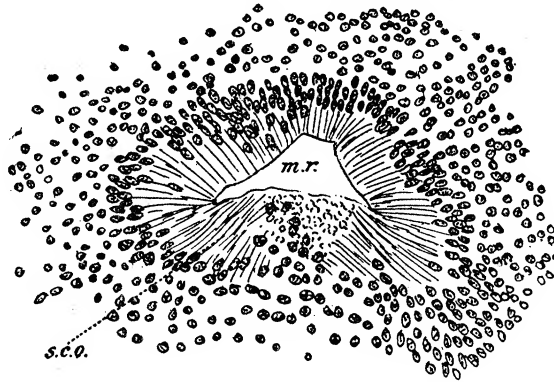


FIG. 9.—Human foetus of about five months. Transverse Section through the Mesocælic Recess, slightly anterior to the section represented in fig. 8. $\times 320$.

m.r., mesocælic recess; *s.c.o.*, sub-commissural organ, forming the epithelial lining of the mesocælic recess.

commissure consists apparently of somewhat flattened cells with conspicuous nuclei, and differs very little from the general lining epithelium of the rest of the *iter*; the only difference being that upon the side walls of the *iter* the nuclei are more crowded, and possibly the epithelium slightly more cubic or columnar, but much less distinctly so than in the foetus. The ependyma beneath the posterior commissure is continuous round the anterior surface of the latter with that which lines the infra-pineal recess, and in no wise differs from it. There is thus upon the surface of the commissure nowhere any indication of that characteristic elongatedly columnar epithelium that marks the sub-commissural organ in lower types.

At the hinder limit of the posterior commissure, however, about the middle line, there is an irregular thickening of the ependymal epithelium, and above this an irregular cavity (Plate 14, fig. 2, *m.r.*) occurs in the tissue of the brain, lined unevenly by the remains of an epithelium, with numerous scattered nuclei, exactly like that on the roof of the *iter* beneath it. No opening could be found putting this cavity into communication with the cavity of the *iter*, but numerous scattered nuclei connect the two epithelia, and suggest the remains of such a communication.

In successive sections this irregular cavity can be traced forwards and upwards, behind and above the posterior commissure. It obviously corresponds to the similarly situated mesocœlic recess in the fœtus, although lacking its characteristic high columnar ependymal lining. Anteriorly it again becomes choked with scattered cells, forming an ill-defined tract which passes forwards and then abruptly gives place to a small, but very well defined, sub-spherical chamber (Plate 14, fig. 3, m.r.). This chamber, moreover, is lined by exactly the same type of elongated epithelium as characterises the sub-commissural organ in the fœtus and in lower forms. The photomicrograph reproduced in Plate 14, fig. 3, shows this chamber, which we regard as simply the blind anterior termination of the mesocœlic recess (compare Plate 14, fig. 1, and text-fig. 9). The lumen here has a diameter of about 0.05 mm., while the cells of the lining epithelium are about 0.02 mm. long, with the nuclei placed as usual towards their inner ends. In the lumen is a small quantity of coagulum.

In the brain tissue around the posterior portion of the mesocœlic recess (*i.e.* that portion where the cavity has become irregular and largely obliterated) occur numerous small globules (Plate 14, fig. 2, gl.) which have stained brightly red in the preparations (which were treated with borax carmine in bulk, followed, upon the slide, by picro-indigo-carmine). Whether these are due to pathological or to *post-mortem* changes we are unable to say; that they are normally present seems improbable—in any case they are conspicuous in these sections, and interesting as occurring closely adjacent to the last vestiges of the sub-commissural organ.

We have thus found the sub-commissural organ fairly well developed in the human fœtus, and in an entirely vestigial condition in the adult. We have, however, only been able to examine one series of sections in each case. Probably, like many other vestigial structures, it will be found to vary considerably in the degree to which it persists in different individuals.

IV. *The Function of the Sub-Commissural Organ and Reissner's Fibre.*

Sargent, who has done so much to extend our knowledge of Reissner's fibre, considered (1904) this structure to be of a nervous nature, forming a kind of short circuit for optic motor reflexes. Our own histological investigations on many types do not support this view, nor do the physiological experiments of Sir Victor Horsley and Dr. McNalty (1908). On the other hand, there is every reason to believe that Reissner's fibre is a highly elastic structure, for it is well known that it has a strong tendency, when cut across, to spring back and coil itself into knots and spirals.*

* Cf. Nicholls (1909).

Moreover, one of us (Nicholls) has been able recently to demonstrate beyond question that at its posterior end (in the lamprey and various teleosts) the fibre is not connected with "canal cells" in the *canalis centralis* of the spinal cord, as maintained by Sargent, but is connected through a terminal foramen in the neural tube with the surrounding connective tissue. Thus Studnička's statements on the subject (1899), controverted by Sargent (1904), are confirmed. At its anterior end the fibre appears always to break up into very slender branches, which are connected with the epithelial cells of the sub-commissural organ.

Reissner's fibre and the sub-commissural organ occur throughout the vertebrate series from the cyclostomes to the primates, and there can be little doubt that where they are (as in nearly all cases) well developed they must have some important function.

In a letter recently published in 'Nature' one of us (Dendy, 1909) has made a suggestion as to the possible function of these organs, which appears to us to be strongly supported by the results recorded in the present communication. This suggestion was to the effect that Reissner's fibre and the sub-commissural organ ("Ependymal Groove") may form part of an apparatus for regulating flexure of the body. It was pointed out that any such flexure would tend to alter the tension of Reissner's fibre, and thereby exert a mechanical stimulus upon the epithelial cells of the sub-commissural organ to which it is attached anteriorly. It was supposed that the stimulus thus received by the sensory epithelial cells might be transmitted to appropriate nerve-cells in the brain, and that the deviations of the long axis of the body from the normal position might thus be regulated by reflex action; and a comparison was made with the function of the semicircular canals of vertebrates, and also with that of the "Statocysts" of many invertebrates, which serve by means of mechanical stimuli, due in this case to the action of gravity, automatically to regulate the orientation of the body.

The fact that man, almost the only vertebrate which has assumed the erect posture, and one of the few which have completely lost the tail, also has the sub-commissural organ in a more reduced condition than in any other case known, while the semi-erect and almost tailless chimpanzee is in this respect in an intermediate condition between man and the lower vertebrates, seems clearly to indicate that the function of the sub-commissural organ is in some way connected with the position of the body and the flexibility of the vertebral column (including of course the tail).

Considering that the sub-commissural organ, with which Reissner's fibre, when present, is invariably connected, is reduced to a mere vestige in the

adult man, it seems extremely improbable that man possesses any Reissner's fibre at all. The only primates in which the presence of Reissner's fibre has yet been demonstrated are *Macacus cynomolgus* and *M. rhesus* (Horsley, 1908), and it is perhaps significant that these are both tailed and non-erect forms.

We may perhaps point out that the suggestion thus put forward as to the possible function of Reissner's fibre and the sub-commissural organ is not inconsistent with the view previously maintained by one of us (Dendy, 1902), to the effect that in the Ammocœte the latter may serve by ciliary action to promote the circulation of the cerebro-spinal fluid.

We should like to express our indebtedness to our colleagues Prof. Waterston, Prof. Peter Thompson, and Mr. Frazer, for placing at our disposal some of the material upon which this paper is based, and Mr. R. W. H. Row for making the photomicrographs used in illustration.

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DESCRIPTION OF PLATE 14.

FIG. 1.—Chimpanzee. Photomicrograph of part of a Transverse Section through the Posterior End of the Posterior Commissure, showing the Sub-commissural Organ and the Mesocœlic Recess. $\times 34$.

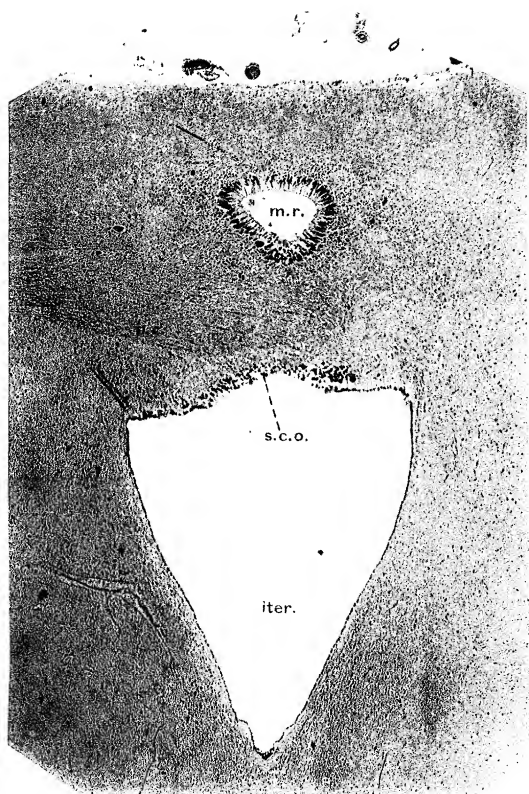


Fig. 1.



Fig. 3.

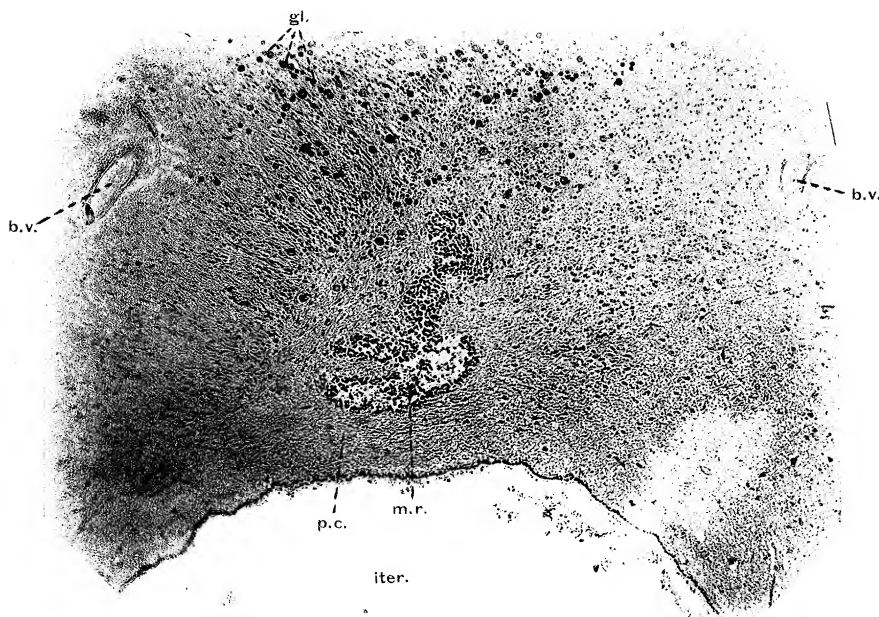


Fig. 2.

FIG. 2.—Man (adult). Photomicrograph of part of a Transverse Section through the Posterior End of the Posterior Commissure, showing the Irregular Proximal (posterior) part of the Mesocœlic Recess. $\times 58$.

FIG. 3.—Man (adult). Photomicrograph of part of a Transverse Section through the Posterior Part of the Posterior Commissure at a level slightly anterior to that of the section represented in fig. 2, to show the terminal (anterior) portion of the mesocœlic recess, with its characteristic columnar epithelium. $\times 300$.

EXPLANATION OF LETTERING.

b. v., blood vessels ; gl., globular bodies ; m. r., mesocœlic recess ; p. c., posterior commissure ; s. c. o., sub-commissural organ.

Autotoxæmia and Infection.

By E. C. HORT, F.R.C.P. Ed., Assistant Physician to the Italian Hospital.

(Communicated by William Osler, F.R.S. Received June 2,—
Read June 23, 1910.)

The object of this communication is to show :—

That fever,* loss of weight, and a rise in the antitryptic values of the blood serum, three results common to infection in man, can be reproduced in animals by the subcutaneous injection of small quantities of distilled water.

CONTROL OBSERVATIONS.

The following precautions were found to be necessary in order to demonstrate these effects, apart from selection of healthy animals for injection, and observance of strict aseptic conditions as to site of injection, instruments used, and water injected :—

Fever.

1. Selection and repeated testing of thermometers of guaranteed accuracy.
2. Accurate approximation of the temperature of the water injected to the temperature of the animal receiving the injection.
3. Determination of the mean average, and of the upper normal limit of, temperature of the species of animal selected for injection.
4. Demonstration that repeated handling and the taking of repeated thermometric observations do not cause a rise of temperature in the control animals.
5. Demonstration that mere subcutaneous puncture, or injection of air equivalent in bulk to the volumes of water injected, does not cause fever in the control animals.

* By fever is here meant a rise of temperature, and nothing more.



FIG. 6.—Chimpanzee. Transverse Section through the Sub-Commissural Organ at the Posterior End of the Posterior Commissure. $\times 60$.

m. r., mesotelic recess; s. c. o., sub-commissural organ.

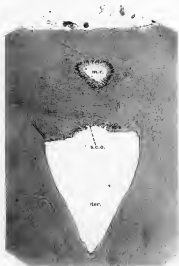


Fig. 1



Fig. 3.

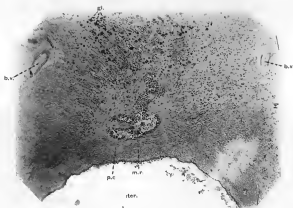


Fig. 2